Correlation of Cystic Fibrosis Related Diabetes with Sensation, Gait Characteristics, and Balance

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ABSTRACT

Objective: To assess if people with cystic fibrosis related diabetes (CFRD) exhibit characteristics of peripheral neuropathy as compared to those with cystic fibrosis alone. Background: Diabetic peripheral neuropathy can cause impaired sensation, gait and balance. It is unknown if CFRD manifests in similar ways. We assessed peripheral nerve function in adults with CFRD (6 M, 1 F, mean age 28 yrs) and adults with CF only (2 M, 1 F, mean age 28 yrs).

Methods and Measures: Light touch, vibration, pinprick, and temperature sensation were tested on both feet, as well as ankle reflex testing as per the Neuropathy Disability Score test. Self-selected gait characteristics (velocity and step length) were assessed via GAITRite computerized walkway. Balance was assessed using the Sensory Organization Test performed on a computerized posturography device.

Results: Sensation was normal in both groups. The CFRD group walked significantly slower (1.18 vs. 1.43 m/sec) and took shorter steps (64 vs. 76 cm) than the CF only group. Both groups scored below population norms on vestibular balance conditions.

Conclusion: CFRD-related peripheral neuropathy, which was undetectable by sensory tests, is related to altered gait and could predispose to falling. CF, or its treatments, may impair balance via vestibular system damage. CFRD adults should be evaluated for peripheral neuropathy and its effects.

Background

Cystic fibrosis related diabetes (CFRD) is the most common comorbidity in adults with CF, affecting 40-50% of patients over the age of 18.¹ The condition of CFRD shares components with both type I and type II diabetes, as there is both insulin deficiency and insulin resistance.² Diabetic peripheral neuropathy is a complication in approximately 50% of both type 1 and type 2 diabetes, and causes impaired sensation, gait changes, and possible balance disruptions.³ Individuals are 2.5 times more likely to have a fall and 15 times more likely to report an injury than those without peripheral neuropathy.⁴,⁵ Much is known about the effects of diabetic peripheral neuropathy and associated functional impairments, but it is not known if CFRD affects peripheral nerves nor what types of impairments CFRD may cause. Therefore, we examined the relationship between CFRD and potential manifestations of peripheral neuropathy including sensation, gait, and balance in a sample of adult patients.

Methods and Measures

This study was approved by the West Virginia University Institutional Review Board.
Board (IRB) and all participants signed informed consent documents prior to testing. Participants were recruited from the Cystic Fibrosis Clinic at West Virginia University. Eligibility criteria included: being at least 18 years of age, with or without CFRD, and medically stable (no symptoms of respiratory infection, such as increased cough/sputum production, or fever) at the time of testing. Exclusion criteria included: a history of transplantation (due to the effect of immunosuppressant drugs on peripheral nerve function), acute pulmonary exacerbation, or cognitive or physical impairments that would affect the ability to walk, stand, or maintain balance. Cognitive impairments were defined as any condition, such as a history of a head injury or intellectual disability, where subjects could not follow testing instructions. Physical impairments included joint injuries or neuromuscular diseases.

**Procedures**

Participants reported to the physical therapy clinic for a single testing session, lasting approximately 45 minutes. To ensure appropriate infection control measures were maintained, each participant was tested individually.

Sensation testing was performed according to the Neuropathy Disability Score procedures, which has been shown to reliably detect peripheral neuropathy. Vibration, pin-prick, ankle reflex, and temperature were tested on both feet, 3 times each. We also performed monofilament testing (5.07/10g) to assess protective sensation.

Spatial and temporal parameters of gait were measured using the GAITRite pressure mapping system (CIR Systems, Inc.; Sparta, New Jersey), a 3 meter long portable walkway imbedded with pressure sensors arranged in a grid pattern. The GAITRite has shown to have excellent reliability and validity for all temporal and spatial measures used in this study. Participants walked barefoot across the pressure mat at a comfortable self-selected pace. They were instructed to start walking 1 meter in front of the mat and to continue walking at the same pace for 1 meter beyond the end of the mat, to exclude effects of acceleration and deceleration on gait parameters. Three trials were recorded to determine gait velocity, step length, base of support, stance time, step length differential, and mean normalized velocity.

Balance was measured using the Sensory Organization Test (SOT) performed on a computerized posturography system (Smart Balance Master, NeuroCom; Clackamas, OR). This system allows separate movement of footplate (surface), walls (surround) or both, depending on the condition. Prior to beginning the SOT, participants stepped barefoot onto the footplate and were fitted into a safety harness in the event of a loss of balance. The participants attempted to maintain static balance in each of the six conditions of SOT:

1. solid support surface with eyes open
2. solid support surface with eyes closed
3. solid support surface, sway referenced surround with eyes open
4. sway referenced support surface with eyes open
5. sway referenced support surface with eyes closed
6. sway referenced support surface, sway referenced surround with eyes open

The test-retest reliability of these conditions is moderate to good (ICC values of 0.42-0.81) in both young subjects and older adults. This test has been used to assess vestibular function in CF patients. Participants completed each condition 3 times and the results, as a percentage of age-predicted norms, were recorded for statistical analysis.
**Statistical Analysis**

Descriptive statistics included mean and standard deviation. The data collected from the sensation testing (correct/incorrect response) were converted into numeric data. Comparisons between CF and CFRD groups were made using independent t-tests. A p-value of <0.05 was considered significant for all tests. As this was an exploratory study, we did not have any preliminary data on which to base a power analysis. Thus, we attempted to enroll all eligible participants who could be tested in the time frame available (approximately 18 months).

**Results**

A total of 10 participants agreed to participate in this study. The CF group (2 male and 1 female) and the CFRD group (6 male and 1 female) each had a mean age of 28 years. The groups did not differ on height (mean 168 cm CFRD vs. 173 cm CF) or weight (mean 60 kg CFRD vs. 67 kg CF).

There were no significant differences between the two groups in the ability to accurately detect any sensation modality tested and there were only rare, scattered incorrect responses. Gait analysis showed a significant decrease in gait velocity in the CFRD group compared to the CF group (1.18 m/sec vs. 1.43 m/sec, see Table 1). The CFRD group also had a significantly shorter step length on the right side (64.49 vs. 75.96 cm). There were no differences between groups in balance, as assessed by the SOT. However, both groups scored well below population norms for condition 5 (means of 55% and 56% respectively, see Table 2). Two participants in the CFRD group and one in the CF group experienced a loss of balance during condition 5, resulting in a need to utilize the safety harness.

**Discussion**

The relationship between CFRD and sensation, gait, and balance has not previously been studied, despite the fact that CFRD is a very common complication in adults with CF. Due to the similarities in pathophysiology between CFRD and other forms of diabetes we sought to determine if patients with CFRD developed the same types of peripheral neuropathic impairments common in the diabetic population. While we did not find that clinical tests of sensation differed between participants with CFRD and those without, we found gait characteristics that suggest possible peripheral nerve impairment in the CFRD group. Participants with CFRD had impaired gait velocity and took shorter steps than those with CF alone. Their mean gait velocity was well below norms for similarly aged healthy persons (1.27 m/sec) and even slower than healthy older adults (1.2-1.5 m/sec). A slower gait speed may require increased balance responses because of the large medial and lateral center of mass displacement that accompanies the decreased velocity when compared to normal walking. Beauchet et al found that as gait speed decreased, gait variability increases making gait more unstable. These changes could result in the increased balance deficits and fall risk in populations with peripheral neuropathies. Whether the gait velocity and step characteristics seen in our participants with CFRD would predispose them to falls was not determined, but would be a good avenue for future study.

We also found that participants with CFRD had a significantly shorter step length on the right side. This may reflect the effects slower gait has on gait variability. While step length on the left was not significantly different between groups, the p-value of 0.07 suggests differences may be detected with a larger sample size.
Table 1. Gait Variables

<table>
<thead>
<tr>
<th>Gait Variable</th>
<th>CF Mean(SD)</th>
<th>CFRD Mean(SD)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gait Velocity (m/sec)</td>
<td>1.43 (0.75)</td>
<td>1.18 (1.37)</td>
<td>0.02*</td>
</tr>
<tr>
<td>Step Length Left (cm)</td>
<td>75.32 (4.19)</td>
<td>64.13 (8.67)</td>
<td>0.07</td>
</tr>
<tr>
<td>Step Length Right (cm)</td>
<td>75.96 (3.07)</td>
<td>64.49 (7.15)</td>
<td>0.03*</td>
</tr>
<tr>
<td>BOS Left (cm)</td>
<td>8.58 (1.98)</td>
<td>11.39 (2.17)</td>
<td>0.09</td>
</tr>
<tr>
<td>BOS Right (cm)</td>
<td>9.05 (2.01)</td>
<td>11.39 (2.11)</td>
<td>0.14</td>
</tr>
<tr>
<td>Stance Time Left (sec)</td>
<td>0.64 (0.03)</td>
<td>0.67 (0.04)</td>
<td>0.16</td>
</tr>
<tr>
<td>Stance Time Right (sec)</td>
<td>0.64 (0.02)</td>
<td>0.67 (0.03)</td>
<td>0.16</td>
</tr>
<tr>
<td>Step Length Differential (cm)</td>
<td>0.99 (0.70)</td>
<td>1.47 (1.37)</td>
<td>0.59</td>
</tr>
<tr>
<td>Normalized Velocity (m/sec)</td>
<td>1.66 (0.24)</td>
<td>1.44 (0.15)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

* indicates significant difference at p < 0.05
BOS = Base of Support

Table 2. Performance on Sensory Organization Test (percentage of age-predicted norm)

<table>
<thead>
<tr>
<th>Condition</th>
<th>CF Mean (SD)</th>
<th>CFRD Mean (SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>94.87 (1.50)</td>
<td>95.57 (2.16)</td>
<td>0.63</td>
</tr>
<tr>
<td>2</td>
<td>93.90 (1.31)</td>
<td>93.47 (2.00)</td>
<td>0.75</td>
</tr>
<tr>
<td>3</td>
<td>94.80 (1.56)</td>
<td>91.99 (3.80)</td>
<td>0.26</td>
</tr>
<tr>
<td>4</td>
<td>88.43 (4.07)</td>
<td>89.56 (4.27)</td>
<td>0.71</td>
</tr>
<tr>
<td>5</td>
<td>55.33 (7.23)</td>
<td>55.99 (26.70)</td>
<td>0.97</td>
</tr>
<tr>
<td>6</td>
<td>76.53 (6.49)</td>
<td>73.47 (13.49)</td>
<td>0.72</td>
</tr>
</tbody>
</table>

Condition 1: eyes open, fixed footplate and surround
Condition 2: eyes closed, fixed footplate
Condition 3: eyes open, moving surround
Condition 4: eyes open, moving footplate
Condition 5: eyes closed, moving footplate
Condition 6: eyes open, moving footplate and surround
Balance deficits and increased fall risk are common in populations with diabetic peripheral neuropathy. While our study did not find significant group differences in balance, a few participants in both groups had a “fall” in the simulated environment under condition 5, which is highly dependent on vestibular input to maintain balance. This suggests that the vestibular system may have been impaired in both groups. Handlesman and colleagues have similarly found impaired vestibular function in CF, as measured by the SOT, despite normal hearing test results. Patients with CF often receive antibiotics to treat pulmonary exacerbations. Some of these medications are known to be ototoxic and it is possible that our participants performed poorly on the tests of vestibular function due to exposure to these antibiotics. As we did not measure antibiotic use or exposure in our participants, we are unable to confirm or refute this hypothesis. Future studies should examine the effects of ototoxic medication use on vestibular function using very sensitive tests such as the SOT.

The limitations in this study include not only lack of documentation of antibiotic medication exposure, but a very small sample size, especially in the CF only group. Despite these limitations, we believe that future study should further examine the relationship between CFRD and peripheral nerve function such as on gait velocity. Further study is also needed on the functional impairments related to impaired vestibular function, such as risk of falling, in adults with CF.

**Conclusion**

We found that CFRD is associated with peripheral neuropathy, particularly in gait velocity and step length. Commonly used clinical tests of peripheral neuropathy, such as sensation testing, appear to be insensitive for detecting these changes, and detailed gait and balance analysis may be necessary to identify subtle impairments. Further case-controlled studies are needed to better identify any effects of CFRD on peripheral nerve function in adults with CF.

**References**


